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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/810,700	03/16/2001	Michael K. Wong	00-149-US	7224

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EXAMINER
CANELLA, KAREN A

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/06/2002 11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/810,700	Wong et al
Examiner	**Art Unit**
Karen Canella	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____ .

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above, claim(s) *21 and 22* is/are withdrawn from consideration.

5) ☒ Claim(s) *8-10, 15, and 16* is/are allowed.

6) ☒ Claim(s) *1-6, 11-14, and 17-20* is/are rejected.

7) ☒ Claim(s) *7* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 9
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Please note that the examiner assigned to this application has changed.

2. Acknowledgment is made of applicants election, with traverse, of Group I, species iii. The traversal is on the grounds that the restriction is improper as the search of species i-v would not be an undue burden to the examiner. This has been considered and found persuasive. The species election requirement of Paper No. 8 is withdrawn.

3. Claims 1-22 are pending. Claims 21 and 22, drawn to non-elected inventions, are withdrawn from consideration. Claims 1-20 are examined on the merits.

Claim Objections

4. Claim 7 is objected to because of the following informalities: The convention of putting a space in between the amino acid residues was not carried out consistently for the amino acid sequence of SEQ ID NO:3.. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 11-14 and 17-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 recites the limitation "therapeutic agent" which lacks antecedent basis in claim 7.

Claim 17 recites the limitation "fragment" which lacks antecedent basis in claim 7.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b).

Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Xu et al (CN 1177005, 1998) as evidenced by Accession Number AAM49503 and Alberts et al (Molecular Biology of the Cell, 1989, pp. 962-963. Claim 1 is drawn to a purified peptide fragment with selective binding to tumor-derived endothelial cells, wherein the peptide fragment possesses a charge motif of positive-positive-neutral, hydrophobic. Accession Number AAM49503 discloses the amino acid sequence of the "inhibitory factor for hyperplasia of inner blood vessel cells in human body's real tumor, and its use in the anti-tumor blood vessel regeneration", which appears to be a direct translation of the title of CN 1177005. The discloses amino acid sequence comprises the claimed motif of positive, positive, neutral-hydrophobic at three positions: residues 62-64, 110-112 and 166-168. As the Accession Number indicates, the polypeptide inhibits hyperplasia of inner blood vessels in a human tumor. Inner blood vessels are endothelial cells as taught by Alberts et al, therefore it is reasonable to assume that the disclosed polypeptide binds to endothelial cell associated with tumors, which is the same as that claimed.

9. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim et al (KR 98073833, 1998) as evidenced by Accession Number AAU77264. The embodiments of claim 1 are set forth above, claim embodies the peptide of claim 1, wherein the peptide is not greater than 50 amino acids in length. Accession number AAU77264 indicates an amino acid sequence of 24

residues which comprises the motif of positive-positive-neutral, hydrophobic at residues 11-13. Table II (page 20207) of The information provided by the Accession Number documentation does not indicate that the disclosed peptides would bind to tumor-derived endothelial cells, however, the disclosed peptide comprises the claimed motif, therefore it is reasonable to assume that it would have the property of binding to tumor-derived endothelial cells. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

10. Claims 1 and 2 rejected under 35 U.S.C. 102(a) as being anticipated by Oh (KR 99081178, 1999) as evidenced by Accession Number AAO20102, or Yoo et al (KR 99032871, 1999) as evidenced by Accession Number AAO14302 or Lee et al (KR 99081421, 1999) as evidenced by Accession Number AAU78102. The embodiments of claims 1 and 2 are recited above. Accession Number AAO20102 indicates an amino acid sequence of 28 residues comprising the claimed motif at residues 3-5 was disclosed by Oh et al. Accession Number AAO14302 indicates an amino acid sequence of 31 residues comprising the claimed motif at residues 23-25 and residues 27-29 was disclosed by Yoo et al. Accession Number AAU78102

indicates an amino acid sequence of 32 residues comprising the claimed motif at residues 5-7 was disclosed by Lee et al. The information provided by the Accession Number documentation does not indicate that the peptide would bind to tumor-derived endothelial cells, however, the disclosed peptide comprises the claimed motif, therefore it is reasonable to assume that it would have the property of binding to tumor-derived endothelial cells. The Office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

11. Claims 1, 3, 4 and 6 are rejected under 35 U.S.C. 102(e) as being anticipated by Godowski et al (US 6,350,450) as evidenced by Accession Number AAE19825, or Goddard et al (US 6,348,359) as evidenced by Accession Number AAE20195. The embodiments of claims 1 and 2 are set forth above. Claim 3 specifically embodies the peptide of claim 1 wherein said peptide is operatively attached to a therapeutic agent capable of selectively exerting a cytotoxic effect on a tumor. Claim 4 embodies the peptide of claim 1 formulated as a pharmaceutical agent. Claim 6 embodies the peptide of claim 1 attached to a diagnostic agent that is detectable upon imaging.

Accession Number AAE19825 indicates that SEQ ID NO:2 of Godowski et al comprises the claimed motif at residues 181-183, 321-323,375-377 and 479-481, which is the TIE ligand NL1 (column 3, lines 19-20). Godowski et al discloses the conjugation of the NL1 ligand with therapeutic and cytotoxic agents, said conjugates useful as anti-tumor agents which specifically target the tumor vasculature (column 2, lines 18-26). Godowski et al disclose pharmaceutical compositions comprising the HL1 ligand (column 30, lines 27-50) and detectably labeled NL1 ligands (column 2, lines 45-49 and column 29, lines 44-51).

Accession Number AAE20195 indicates that SEQ ID NO:2 of Goddard et al comprises the claimed motif at reside 71-73, 121-123, 128-130, 150-152, 163-165 and 182-184, wherein said SEQ IS NO:2 is the TIE ligand NL2 (column 3, lines 24-25). Goddard et al discloses the conjugation of the NL2 ligand with therapeutic and cytotoxic agents, said conjugates useful as anti-tumor agents which specifically target the tumor vasculature (column 2, lines 22-30). Goddard et al disclose pharmaceutical compositions comprising the NL2 ligand (column 29, line 58 to column 30, line 14) and detectably labeled NL2 ligands (column 2, lines 49-53 and column 29, lines 9-15).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1, 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Godowski et al (US 6,350,450) in view of Thorpe et al (US 5,965,132), or Goddard et al (US 6,348,359) in view of Thorpe et al (US 5,965,132). The embodiments of claims 1, 3, 4 and 6 are set forth above.

Godowski et al or Goddard et al teach the embodiments of claims 1, 3, 4 and 6 for the reasons set forth above. Neither Godowski et al nor Goddard et al specifically teach a therapeutic agent capable of inducing tumor necrosis as a cytotoxic effect.

Thorpe et al teach therapeutic agent constructs which localize to the tumor vasculature and result in tumor necrosis (column 4, lines 38-48). Thorpe et al specifically teach anti-tumor endothelial cell antibodies conjugates to ricin (column 55, "Example II, especially column 56, line 57 and column 59, lies 17-31).

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to use ricin as the cytotoxic agent in the conjugates of NL1 and NL2 as disclosed by Godowski et al and Goddard et al, respectively. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Thorpe et al on the ability of therapeutic agents comprising tumor vasculature targeting agents conjugated to ricin to induce tumor necrosis.

Conclusion

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.

Patent Examiner, Group 1642

November 4, 2002